THE RESPIRATORY EXCHANGE OF MICE BEARING TRANSPLANTED CARCINOMA.¹

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ALTHOUGH in the last few years much experimental work has been done on animals inoculated with various forms of malignant tumour, the only work on the gaseous metabolism in such animals that has so far been published is that of Cramer (1908¹), who used rats inoculated with a spindle-celled sarcoma. The object of the present research was to determine whether the presence of transplanted carcinomatous tumours in mice caused any alteration in the respiratory exchange of the animals. Attention was directed rather to the respiratory quotient than to the actual amount of CO₂ produced and O₂ absorbed, as the latter varies within wide limits with the activity of the animal.

The mice which were the subjects of the following experiments were inoculated with small pieces of a Jensen-mouse carcinoma, series $\frac{1}{5}$, kindly given me by Dr. Paine, Director of the Research Laboratories of the Cancer Hospital. The inoculations were made under the skin of the right flank with a Bashford's hollow needle, and, the tumour being in a positive phase of growth, were successful in a large percentage of cases (100 per cent. in series $\frac{1}{5}$), the tumour growing quickly with large areas of necrosis. The apparatus used for the determination of the respiratory exchange was that described by Haldane (1892²) and Pembrey (1893³); and the precautions advised by them were all adopted, including the weighing of the tubes and animal chamber against a dummy tube and chamber, and the insertion of control tubes. The weighings were done on a balance weighing to 0.1 mg., but no attempt was made to weigh beyond 0.5 mg. In the preliminary experiments the animal chamber was exposed to the air of the laboratory, the temperature of which was usually about 10–12° C., with the consequence that the animal was extremely active at first, but became quieter as the temperature in the chamber rose; the absorption of O₂ and excretion of CO₂ therefore varied very considerably. To eliminate this source of variation, the animal chamber, in the recorded experiments, was immersed in a water bath at a constant temperature of 20–21° C., which in the later experiments was raised to 22–23° C. The result was, on the whole, satisfactory, though occasionally the animal became very active, with the result of an increased production of CO₂ and absorption of O₂. Four sets of apparatus were used at the same time, and so far as possible the experiments on the inoculated animals and the control animals were made at the same time. The animals in all cases except in the feeding experiments were fed about 5 p.m. on the previous day, and then received no further food till after the experiment, and were thus in a fasting state. Except in the case of the feeding experiment, each experiment lasted four hours. The measurements given for the tumour

¹ Received August 8, 1910.

throughout the experiments are those of, the greatest length, breadth, and depth, but owing to the irregular shape of the tumour they can only serve as a rough guide to its volume. The observed measurements are obviously too high; but, taking all the available measurements of the various tumours, and comparing them with the weights after removal or after death, it seems that the volume of the tumour in c.c. calculated on the assumption that it is a cube, is three times its weight in grammes. The variations in the size and shape of the tumours are, however, so great that this correspondence must be only very approximate, and is not accurate enough to allow any calculations to be based upon it.

The experiments fall into three groups. (1) The first group dealing with the respiratory exchange of the inoculated and the control animals; (2) the second group showing the effect of the removal of the tumour; (3) the third group dealing with the effect of feeding. For details see pp. 199–206.

SERIES I. (Nos. I., II., III., IV., VI., XIII., XVI., XVII., XIX., XX.—The results for mouse I., though experiment 8 gives a very high result, probably due to unusual activity, give an average which is in close agreement with the results for normal mice given by Oddi (1891⁴), and by Pembrey (1893⁵), and also with the results for mouse II., which was suffering from a tumour. As mouse II. was found dead the day after the last experiment, and the animal without the tumour weighed 21 grms., giving 8 grms. as the weight of the tumour, it may be of interest to calculate the exchange for the animal and the non-necrotic part of the tumour from the figures found for 11th February, the date of the last experiment. The necrotic area is assumed to be 75 per cent. of the whole, this being roughly the amount of necrosis usually found in this strain of tumour. (It was impossible actually to measure the necrotic area in this case, as when the mouse was found dead most of the growth had been eaten away.) This gives the weight of the animal and the non-necrotic part of the tumour as 23 grms., and the CO₂ per kilo per hour as 8.78 grms., the O₂ being 8.87 grms., which is almost exactly the same result as was given by the control animal (CO₂, 8.70 grms.; O₂, 8.93 grms.). In mouse III. 50 per cent. of the tumour was necrotic; this gives for the weight of the animal and the non-necrotic portion of the tumour on 4th February, 22.5 grms. From this the CO₂ per kilo of living tissue per hour was 9.07 grms., and the O₂, 9.63 grms., which are very near the figures for the control mouse IV. (CO₂, 8.55; O₂, 8.63 grms.). If it were possible to make a similar calculation for the other results given by mouse III., it seems probable that the difference between the figures for the tumour-bearing mouse and those for the control mouse would practically disappear. As it is, the figures for the control are rather higher than those for the tumour mouse; but the latter had a large tumour, which was probably necrotic almost from the first, as necrosis was found in quite small and young tumours of this series.

Mouse VI. was inoculated on 3rd December 1909, but never developed a lump larger than a pin's head, which was probably inflammatory and not a true carcinomatous mass. It disappeared by 22nd February, and the figures for the experiments show nothing abnormal.

Animals XVI., XVII., XIX., XX. show no constant difference in the respiratory exchange between animals with tumours and those of the same breed and age without tumours. As the animals were not killed till a few days after the last experiment, during which time the tumour increased rapidly in size, no calculations such as were made above are possible. As it is, the figures for mouse XVII. (CO₂, 6.89 grms.; O₂, 6.84 grms.; R. Q., 0.73) are almost identical with those for mouse XIX. (CO₂, 6.91 grms.; O₂, 6.71 grms.; R. Q., 0.75), and those for mice XVI. and XX. are within the limits for normal mice.

TABLE OF AVERAGES.

Tumour Mice.				Mice without Tumours.			
Number.	CO ₂ grms. per Kilo per Hour.	O ₂ .	R. Q.	Number.	CO ₂ .	O ₂ .	R. Q.
Mouse II.	7.85	8.20	0.69	Mouse I.	8.70	8.93	0.70
„ III.	6.84	7.06	0.71	„ IV.	8.55	8.63	0.72
„ XVI.	7.18	7.08	0.74	„ VI.*	6.04	6.15	0.71
„ XVII.	6.89	6.84	0.73	„ XIX.*	6.91	6.71	0.75
„ XIII.	6.96	6.79	0.73	„ XX.*	8.50	8.31	0.74
Averages	7.14	7.19	0.72	Averages	7.74	7.75	0.73

* These animals were inoculated, but never developed a tumour.

The average weight of the tumour (6.5 grms.) was 24 per cent. of the average weight of the animal and the tumour (27 grms.). Taking the necrosis as 75 per cent. of the tumour per kilo of live tissue, therefore the tumour mice had an exchange of 8.7 c.c., *i.e.* 13 per cent. more than the controls; making no allowance for necrotic tumour substance, their exchange was $7\frac{1}{2}$ per cent. lower; but it must be remembered that the estimate of the percentage of necrotic tissue is only a rough one.

After death the animals were examined for the presence of secondary deposits, and notes as to the conditions found are placed at the end of the tables in the protocols. Mouse XVI. is interesting from another point of view, from the fact that its kidneys contained the parasite *Klossiella muris*, first described by Smith and Johnson, (1902⁶) and afterwards by Woodcock (1904⁷), and kindly identified for me by the latter writer. The parasite was also found in the kidneys of mice VIII., IX., X., and XIV. All these mice were from the same batch, but the last five lived in one cage together, while No. XVI. lived in a different cage.

Lubarsch (1910⁸) drew attention to the frequency of amyloid changes in the organs of carcinomatous white mice, and after his paper appeared all the organs were examined for such changes; they were, however, only found once (mouse IX.), and then only to a slight degree. Possibly this is due to the fact that Lubarsch worked with white mice, while all mine, with one exception, were coloured, and that the average size of his tumours was considerably greater than that of the tumours in my animals.

SERIES II.—*The effect of removal of the tumours* (mice VII., VIII., IX., X., XI., XII.). In six animals the tumour was removed under ether anæsthesia, after preliminary observations on the respiratory exchange.

The sixth mouse (No. XIII.) was found dead the day after the operation, and the experiments made on it before the removal of the tumour are

included in Series I. The other five mice recovered from the operation, though all eventually suffered from recurrence. This was to be expected from the necrotic nature of the tumour, which made it difficult to remove it entire, and without soiling the wound with cancer cells.

In all these cases there was a definite rise in the amount of CO_2 excreted and O_2 absorbed, though not in the respiratory quotient at the first experiment after the operation. The explanation would seem to be that, before removal, there is included in the weight of the animal a considerable amount of necrotic tumour tissue, which takes no part in the respiratory exchange, while after removal the body weight is entirely formed of living tissue. That this explanation is the true one may be seen by comparing the averages before and after removal in the case of mice IX. and VIII. In the former cases experiments were made after the tumour had recurred, and the average figures for the CO_2 (before removal 7.89 grms., after 7.46) and O_2 (before 8.32, after 7.33) before and after removal are not very different; while in the latter case no experiments were made after the recurrence of the tumour, and the averages after the operation (CO_2 , 8.48 grms.; O_2 , 8.52) are higher than those before (CO_2 , 6.98; O_2 , 6.81). The general result of the figures for animals X. and XI. is to the same effect, though it does not appear in the average figures, owing to the fact that the first experiment in the first case, and the first two experiments in the second case, were performed when the mice were obviously very ill, and therefore gave low results. The figures for animal VII. are somewhat inconclusive, but the averages include very high figures (experiment 3) and very low figures (experiment 10).

SUMMARY OF RESULTS OF REMOVAL.

Number.	Operation.	CO_2 per Kilo per Hour.	O_2 per Kilo per Hour.	R. Q.
Mouse VII.	Before	6.71	6.68	0.73
	After	6.12	5.82	0.76
„ VIII.	Before	6.98	6.81	0.75
	After	8.48	8.52	0.73
„ IX.	Before	7.89	8.32	0.69
	After	7.46	7.33	0.74
„ X.	Before	5.81	5.86	0.72
	After	7.07	6.97	0.74
„ XI.	Before	4.51	4.58	0.72
	After	7.01	6.99	0.73

SERIES III.—*Feeding Experiments.* It is well known that there is a marked rise in the respiratory quotient after a meal rich in carbohydrates; and that this rise is due to an increase in the excretion of CO_2 , the absorption of O_2 remaining at about the same level. It has been shown by Pembrey and Spriggs

(1904⁹), in the case of rats, that this rise persists for several hours after the meal, and has been interpreted by them, and also by Hanriot (1892¹⁰), as being the result of the transformation of carbohydrates into fats, CO_2 being split off. Cramer (*loc. cit.*) has shown that in rats with sarcomatous tumours the rise in CO_2 excretion is neither so great nor so persistent as in normal rats, and concludes that the needs of the tumour do not permit of the storing of the excess of carbohydrates as fat, and that "such a storing of the absorbed food material in the form of fat does not take place at all, or not to the same extent as in normal animals." In my experiments the animals received a meal about 10 a.m. on the morning of the day before the experiment (Figs. 1-5). On the morning of the experiment an observation was first made, except in the case of mouse XIV., while the animal was in a fasting condition; it was then fed on bread soaked in water for fifty minutes, and hourly determinations were made till the quotient dropped to the fasting level. The effect of the meal was to produce a considerable rise in the excretion of CO_2 , the absorption of O_2 (except in the case of mouse XXII, Fig. 5) remaining at or above the same figures. The curve constructed from the observations shows a slightly greater rise, and greater persistence of the rise, in the respiratory quotient in the case of the normal mice as compared with the tumour animals, but the difference is not marked. This is probably due to the more vigorous metabolism of the mouse as compared with the rat, for it is well known that the metabolism of small warm-blooded animals is greater in proportion to their size than it is in larger animals. It would seem that the normal metabolism of the mouse is so great that it allows of very little storage of excess of carbohydrate food, and I have found that mice bear deprivation of food very badly.

FIG. 1.—Mouse xv. : no tumour.

FIG. 2.—Mouse XV. : no tumour.

FIG. 3.—Mouse XX. : no tumour.

FIG. 4.—Mouse XIV. : tumour.

FIG. 5.—Mouse XXII. : tumour.

CONCLUSIONS.

(1) There is no marked difference in the respiratory exchange of mice with tumours and normal mice, if allowance be made for the necrosis of the tumour.

(2) Removal of the tumour produces no marked effect on the respiratory exchange, if allowance be made for the necrosis.

(3) After a meal of carbohydrate the rise in the respiratory quotient and the excretion of CO_2 is slightly greater in the mice with tumours than in the normal mice, but the difference is not marked.

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MOUSE I.—Dark brown Female. Not Inoculated.

Number.	Date.	Temperature.	Time.	Weight.	H ₂ O.	CO ₂ found.	Per Kilo per Hour.	O ₂ found.	Per Kilo per Hour.	R. Q.	
1	Jan. 4	22.5	12.0-4.0	grs. 27	grms. 0.4430	grms. 0.5485	grms. 5.04	grms. 0.5335	grms. 5.40	0.69	
2	" 14	20.5	11.35-3.35	23	0.7310	0.8395	9.12	0.9655	10.49	0.63	
3	" 18	21	10.35-2.35	21.2	0.3775	0.6350	7.49	0.6505	7.67	0.71	
4	" 22	22.5	9.45-1.45	20	0.3855	0.5470	6.84	0.5525	6.92	0.72	
5	Feb. 2	22.5	11.12-3.12	21.8	0.3220	0.6105	7.00	0.6345	7.28	0.70	
6	" 4	22.5	11.50-3.50	23.6	0.9800	0.6820	7.24	0.6770	7.16	0.73	
7	" 9	22	11.35-3.35	22.8	0.3690	0.6240	6.84	0.6540	7.17	0.70	
8	" 11	22	11.5-3.5	24.6	0.8650	1.3855	14.1	1.3815	14.0	0.73	
9	" 12	22.5	9.55-1.55	22.2	0.4650	0.5890	6.41	0.5440	6.13	0.76	
10	" 16	22.5	11.25-3.25	23	0.3290	0.5870	6.88	0.5970	6.49	0.71	
11	" 18	22	11.43-3.43	23	0.4455	0.6145	6.67	0.6130	6.66	0.73	
12	" 22	22.5	12.17-4.17	25.7	1.1550	1.0030	9.75	1.0230	9.95	0.71	
Average				23.2		0.7205	8.70	0.7398	8.93	0.70	

MOUSE II.—Black Female. Inoculated October 29, 1909. Series $\frac{1}{3}$. Same Generation as I.

Number.	Date.	Temperature.	Time.	Weight.	H ₂ O.	CO ₂ found.	Per Kilo per Hour.	O ₂ found.	Per Kilo per Hour.	R. Q.	Tumour.
1	Jan. 11	21	11.8-3.8	grs. 25.5	grms. 0.7825	grms. 0.8340	grms. 8.17	grms. 0.9065	grms. 8.91	0.67	1 cm.
2	" 12	21	11.0-3.0	21.5	0.9585	0.7475	8.69	0.7640	8.88	0.71	2.2×1.8×0.8
3	" 14	20	10.55-2.55	22.5	0.4680	0.6590	7.32	0.7305	8.12	0.66	2.5×2×1.5
4	" 22	22.5	10.17-2.17	23.4	0.3875	0.6945	7.42	0.6935	7.41	0.73	2.8×2.2×1.8
5	Feb. 2	22.5	10.28-2.28	24.4	0.3400	0.7920	8.11	0.8000	8.20	0.72	3×2.3×2.3
6	" 5	22	10.10-2.10	28.2	0.7080	0.9605	8.42	0.9475	8.31	0.74	3×2×2.5
7	" 9	22	11.0-3.0	28.9	0.5035	0.8845	7.65	1.0050	8.70	0.64	Just ulcerating.
8	" 11	22	10.20-2.20	29	0.4535	0.8080	6.97	0.8165	7.04	0.72	3.2×2.3×3.5
Average				25.4		0.7975	7.85	0.8333	8.20	0.69	Ulcerating.

February 12.—Found dead. Growth mostly eaten away. Weight of mouse less tumour=21 grms.; 2 tape-worms in liver; large spleen. Small secondary deposits in both kidneys. No amyloid change in liver, spleen, or kidneys.

MOUSE III.—*Black and white Female. Inoculated December 3, 1909.*
Series 1.

Number.	Date.	Temperature.	Time.	Weight.	H ₂ O.	CO ₂ found.	Per Kilo per Hour.	O ₂ found.	Per Kilo per Hour.	R. Q.	Tumour.
1	Jan. 15	21.5	10.45-2.45	grs.	grms.	grms.	grms.	grms.	grms.		cms.
2	" 19	22	11.40-3.40	20.5	0.2240	0.6170	7.72	0.6085	7.61	0.74	2.3×1.5×1.3
3	" 21	23	11.55-3.55	19.8	0.2065	0.6115	7.11	0.6130	7.11	0.72	2.5×1.5×1.5
4	" 25	22.5	10.50-2.50	20.6	0.5520	0.5260	6.64	0.5635	7.12	0.68	2.8×1.3×2
5	" 31	22	11.50-3.50	26.5	0.2985	0.4290	5.20	0.4455	5.40	0.70	3×2×2
6	Feb. 2	22.5	12.3-4.3	26.8	0.4775	0.7310	6.90	0.7380	6.91	0.72	Just ulcerating.
7	" 4	22.5	11.6-3.6	27.5	0.6380	0.7350	6.86	0.7725	7.20	0.69	3.2×2×2.4
					1.0245	0.8160	7.42	0.8665	7.88	0.69	4.2×.8×3.3
											4×3.33×.5
											Tumour bleeding.
Average				23.3		0.6379	6.84	0.6585	7.06	0.71	

February 4.—Killed. Looked ill and wasted. Weight of mouse less tumour=17 grms. Weight of tumour=10 grms. About 50 per cent. necrotic. No secondaries in the organs.

MOUSE IV.—*Sandy-white Male. Not inoculated. Same Generation as III.*

Number.	Date.	Temperature.	Time.	Weight.	H ₂ O.	CO ₂ found.	Per Kilo per Hour.	O ₂ found.	Per Kilo per Hour.	R. Q.	
1	Jan. 15	21.5	11.15-3.15	grs.	grms.	grms.	grms.	grms.	grms.		
2	" 21	23	10.55-2.55	21	1.4005	0.7575	8.61	0.8280	9.41	0.67	
3	" 25	22.5	10.10-2.10	19	0.4410	0.5475	7.20	0.5525	7.40	0.72	
4	" 31	22	12.25-4.25	17.5	0.6190	0.7870	11.20	0.7850	11.20	0.73	
5	Feb. 4	22.5	10.25-2.25	22.6	0.7235	0.6495	7.17	0.6750	7.46	0.70	
6	" 8	22.5	11.45-3.45	24.2	0.5915	0.7100	7.33	0.7470	7.71	0.69	
7	" 16	22.5	10.55-2.55	22.6	0.4330	0.6065	7.70	0.7325	8.10	0.69	
8	" 18	22.5	11.18-3.18	21.3	0.5515	0.7900	9.34	0.7955	9.34	0.73	
9	" 23	22.5	10.20-2.20	21.3	0.5240	0.8905	12.12	0.8805	10.9	0.74	
10	" 26	22.5	10.20-2.20	22.5	0.5280	0.7530	8.42	0.6840	7.60	0.80	
				19.4	0.7580	0.6525	8.40	0.6365	8.20	0.74	
Average				21.2		0.7245	8.55	0.7316	8.63	0.72	

MOUSE VI.—*Sandy-brown Female. Inoculated December 3, 1909. Series 1.*

Number.	Date.	Temperature.	Time.	Weight.	H ₂ O.	CO ₂ found.	Per Kilo per Hour.	O ₂ found.	Per Kilo per Hour.	R. Q.	
1	Feb. 11	22	12.21-4.21	grs.	grms.	grms.	grms.	grms.	grms.		
2	" 15	22.5	10.53-2.53	24.5	0.7735	0.6310	6.24	0.6465	6.60	0.71	
3	" 17	22.5	10.58-2.58	25.5	0.3475	0.6210	6.08	0.6310	6.16	0.72	
4	" 22	22.5	10.52-2.52	24.6	0.3530	0.6530	6.64	0.6570	6.68	0.72	
5	Mar. 2	23	10.55-2.55	23.5	0.3270	0.5985	6.36	0.6085	6.47	0.69	
6	" 8	23	11.27-3.27	24.1	0.5945	0.6420	6.66	0.6345	6.58	0.72	
7	" 12	23	10.26-2.26	22.5	0.5990	0.4160	4.62	0.4230	4.70	0.72	
				25.3	0.3255	0.5490	5.42	0.5855	5.78	0.68	
Average				24.3		0.5872	6.04	0.5980	6.15	0.71	

This mouse never developed a lump larger than a pin's head, which was probably inflammatory, and not a true carcinomatous tumour.

RESPIRATORY EXCHANGE IN MOUSE CARCINOMA. 201

MOUSE XIII.—Black Male. Inoculated February 26, 1910. Series $\frac{1}{3}$.

Number.	Date.	Temperature.	Time.	Weight.	H ₂ O.	CO ₂ found.	Per Kilo per Hour.	O ₂ found.	Per Kilo per Hour.	R. Q.	Tumour.
1	Mar. 16	23	11.12-3.12	grs. 25.8	grms. 0.3870	grms. 0.7070	grms. 6.85	grms. 0.6850	grms. 6.63	0.75	1.8×1×1.2
2	" 19	23	10.10-2.10	23.5	0.2905	0.5900	6.28	0.5945	6.32	0.72	2×1.2×1.2
3	" 23	23	12-4	24.4	0.3200	0.6360	6.52	0.6280	6.43	0.74	2.2×2×1.5
4	" 30	23	12.5-4.5	21.2	0.4955	0.6090	7.89	0.6705	7.91	0.72	3×2×1.8
Mar. 31.—Weight of mouse less tumour=18.7 grms. Tumour, 2.5 grms. Removed under ether. Not adherent.											
Average				23.7		0.6505	6.96	0.6445	6.79	0.73	
April 1.—Found dead. Large areas of central necrosis of the liver. No secondary deposits and no amyloid change.											

MOUSE XVI.—Black Female. Inoculated February 26, 1910. Series $\frac{1}{3}$.

Number.	Date.	Temperature.	Time.	Weight.	H ₂ O.	CO ₂ found.	Per Kilo per Hour.	O ₂ found.	Per Kilo per Hour.	R. Q.	Tumour.
1	April 12	23	10.5-2.5	grs. 22.5	grms. 0.4540	grms. 0.4010	grms. 4.46	grms. 0.4000	grms. 4.44	0.73	2.5×1.72×.5
2	" 15	23	10.40-2.40	22.2	0.4280	0.5335	6.06	0.5465	6.21	0.71	2.5×2×1.5
3	" 19	23	11.9-2.9	23.1	0.6720	0.5540	5.99	0.5400	5.84	0.74	3×2×1.7
4	" 22	23	10.0-2.0	24.2	0.7885	0.7860	8.12	0.7935	8.19	0.72	3×2.2×1.8
5	" 26	23	11.11-3.11	23.9	0.4890	0.8970	9.38	0.8750	9.15	0.74	3×2.2×2
6	May 3	23	10.5-2.5	25.1	1.3810	0.8790	8.75	0.8410	8.37	0.76	3×2.5×2.3
Average				23.5		0.6751	7.18	0.6660	7.08	0.74	
May 7.—Very ill. Killed with CHCl ₃ . Mouse less tumour=22.6 grms. Tumour=7 grms. Alveolar carcinoma. No secondary deposits and no amyloid change. <i>Klossiella muris</i> in kidneys.											

MOUSE XVII.—Sandy-white Male. Inoculated February 26, 1910. Series $\frac{1}{3}$.

Number.	Date.	Temperature.	Time.	Weight.	H ₂ O.	CO ₂ found.	Per Kilo per Hour.	O ₂ found.	Per Kilo per Hour.	R. Q.	Tumour.
1	April 12	23	10.45-2.45	grs. 25.4	grms. 0.7295	grms. 0.6490	grms. 6.38	grms. 0.6585	grms. 6.48	0.72	2.21×.5×1.2
2	" 15	23	10.0-2.0	22.1	0.3680	0.6090	6.59	0.6200	7.01	0.71	Ulcerating.
3	" 19	23	10.47-2.47	22.4	0.9745	0.7360	8.21	0.7305	8.15	0.73	2.5×1.5×1.2
4	" 26	23	10.20-2.20	23.3	0.7665	0.6750	7.24	0.6265	6.72	0.78	Deep ulcer.
5	" 29	23	10.10-2.10	23.2	0.4800	0.5880	6.34	0.6110	6.58	0.70	3×1.51×.5
6	May 3	23	10.35-2.35	23.8	0.5940	0.6140	6.46	0.5970	6.27	0.75	4×2×1.6
Average				23.4		0.6452	6.89	0.6406	6.84	0.73	4×2.3×2.2
May 6.—Very ill. Killed with CHCl ₃ . Mouse less tumour=23 grms. Tumour=5 grms. Tape-worm cyst in liver. Mixed alveolar and acinous carcinoma. No secondary deposits and no amyloid change.											

MOUSE XIX.—*Grey-white Male. Inoculated February 26, with no Result.*

Number.	Date.	Temperature.	Time.	Weight.	H ₂ O.	CO ₂ found.	Per kilo per Hour.	O ₂ found.	Per kilo per Hour.	R. Q.	
1	April 12	23	11.54-3.54	grs. 19.2	grms. 0.5880	grms. 0.4170	grms. 5.43	grms. 0.4200	grms. 5.47	0.72	
2	" 15	23	11.12-3.12	21	0.6410	0.6175	7.35	0.5835	0.95	0.77	
3	" 19	23	9.55-1.55	21.4	0.6615	0.6235	7.28	0.6580	7.08	0.69	
4	" 26	23	12.5-4.5	21.7	0.8490	0.5725	6.59	0.5465	6.29	0.76	
5	May 3	23	11.15-3.15	21.5	1.1115	0.6470	7.52	0.6055	7.04	0.77	
6	" 6	23	10.20-2.20	22.6	0.5370	0.6530	7.22	0.6180	6.83	0.77	
Average				21.3		0.5884	6.91	0.5719	6.79	0.75	

MOUSE XX.—*Grey and white Male. Inoculated February 26, with no Result.*

Number.	Date.	Temperature.	Time.	Weight.	H ₂ O.	CO ₂ found.	Per kilo per Hour.	O ₂ found.	Per kilo per Hour.	R. Q.	
1	April 20	23	11-3	grs. 18.8	grms. 0.5330	grms. 0.3900	grms. 11.83	grms. 0.8720	grms. 11.59	0.74	
2	" 22	23	11.33-3.33	18.9	0.2910	0.5700	7.65	0.5640	7.46	0.74	
3	" 26	23	11.40-3.40	19.1	0.6720	0.5980	7.83	0.5710	7.47	0.76	
4	" 29	23	11.25-3.25	19.1	0.5510	0.4800	6.27	0.4820	6.31	0.74	
5	May 4	23	10.32-2.32	20	0.3890	0.7930	9.91	0.7720	9.65	0.74	
6	" 6	23	10.50-2.50	20.4	0.3830	0.6610	7.37	0.5990	7.34	0.73	
Average				19.4		0.6580	8.50	0.6433	8.31	0.74	

MOUSE VII.—*Sandy Male. Inoculated December 3, 1909. Series 1.*

Number.	Date.	Temperature.	Time.	Weight.	H ₂ O.	CO ₂ found.	Per Kilo per Hour.	O ₂ found.	Per Kilo per Hour.	R. Q.	Tumour.
1	Feb. 15	22.5	10.15-2.15	36	grms. 0.3125	grms. 0.9465	grms. 6.57	grms. 0.9310	grms. 6.46	0.74	{ ens. Tumour size of pea. 2×1.5×1.5 2.5×1.8×2 2.3×2×2
2	" 17	22.5	10.30-2.30	34.5	0.2720	0.8665	6.21	0.8285	6.00	0.76	
3	" 22	22.5	10.10-2.10	34.4	0.6310	1.3800	10.03	1.3880	10.09	0.72	
4	" 23	22.5	10.50-2.50	33.7	0.6615	0.8640	6.48	0.8485	6.29	0.74	
5	" 25	23	11.23-3.22	33.1	0.3695	0.7180	5.42	0.7365	5.56	0.71	
6	Mar. 1	23	12.15-4.15	30.4	0.6375	0.6560	5.39	0.6755	5.55	0.71	
" 19. Tumour=5 grms. Removed under ether. Necrotic. Not adherent.											
7	" 23	23	11.35-3.35	24.8	0.7840	0.7670	7.73	0.7175	7.23	0.77	Small pea tumour.
8	" 29	23	10.50-2.50	23.7	0.3940	0.6550	6.91	0.6305	6.65	0.75	
9	April 2	23	9.50-1.50	29	0.6065	0.7480	6.45	0.6985	6.02	0.78	
10	" 8	23	9.55-1.55	24.5	0.7310	0.3255	3.32	0.3265	3.33	0.72	
Average before removal				33.7		0.9052	6.71	0.9013	6.68	0.73	
" after removal				25.5		0.6239	6.12	0.5932	5.82	0.76	

April 20.—Found dead. Large tumour. Secondary deposits in peritoneum and lungs. This animal had been treated by Dr. E. Bellingham-Smith with solution of radium emanations by the mouth before the first experiment. The last dose was given on February 11.

MOUSE VIII.—*Grey and white Male. Inoculated February 7. Series 1.*

[illegible]

MOUSE IX.—*Sandy Male. Inoculated February 7. Series 1.*

[illegible]

MOUSE XV.—*Sandy Male. Not Inoculated.*

Number.	Date.	Temperature.	Time.	Weight.	H ₂ O.	CO ₂ found.	Per Kilo per Hour.	O ₂ found.	Per Kilo per Hour.	R. Q.
1	Apr. 13	23	10-11	grs.	grms.	grms.	grms.	grms.	grms.	0.73
2	" 13	23	11.45-12.45	24.4	0.3290	0.1876	7.68	0.1866	7.64	0.73
3	" 13	23	12.45-1.45	24.9	0.1830	0.2735	10.98	0.2155	8.96	0.92
4	" 13	23	1.45-2.45	24.7	0.2550	0.2060	8.24	0.1710	6.92	0.88
5	" 13	23	2.45-3.45	24.4	0.2310	0.1695	6.95	0.1635	6.70	0.75
6	" 13	23	3.45-4.45	24.2	0.1120	0.1285	5.31	0.1245	5.56	0.70
7	May 4	23	10.5-11.5	24.1	0.0660	0.1240	5.56	0.1370	5.68	0.71
8	" 4	23	11.55-12.55	21.9	0.0675	0.1360	6.16	0.1355	6.19	0.72
9	" 4	23	12.55-1.55	23.6	0.2470	0.2470	10.55	0.1450	6.17	1.23
10	" 4	23	1.55-2.55	23.1	0.7845	0.2250	9.74	0.1735	7.51	0.94
11	" 4	23	2.55-3.55	23.3	0.2690	0.1500	6.72	0.1640	7.35	0.67
12	" 4	23	3.55-4.55	22.1	0.1100	0.1210	5.48	0.1830	6.01	0.66
				22	0.3080	0.2040	9.27	0.2270	10.32	0.65

April 12 - Fed 10-11 a.m.

April 13 - Fed 11.5-11.40 a.m.

May 2 - Fed 9.30-10.30 a.m.

May 4 - Fed 11.8-11.50 a.m.

MOUSE XX.—*Grey and white Male. Inoculated February 26. Series $\frac{1}{3}$ A.*
Never had tumour.

Number.	Date.	Temperature.	Time.	Weight.	H ₂ O.	CO ₂ found.	Per Kilo per Hour.	O ₂ found.	Per Kilo per Hour.	R. Q.
				grs.	grms.	grms.	grms.	grms.	grms.	
1	May 11	23	10.5-11.5	15.5	0.0700	0.0860	4.57	0.0990	6.38	0.63
2	" 11	23	11.55-12.55	16.7	0.1320	0.1420	8.50	0.1090	5.98	0.95
3	" 11	23	12.55-1.55	16.6	0.3780	0.5500	2.54	0.1170	7.05	0.93
4	" 11	23	1.55-2.55	16.2	0.2380	0.0955	5.39	0.0895	5.53	0.73
5	" 11	23	2.55-3.55	15.9	0.0550	0.0450	2.33	0.0480	3.02	0.68

May 10—Fed 11.5-11.50 a.m. May 11—Fed 11.5-11.50 a.m. After first observation.

MOUSE XIV.—*Grey and white Female. Inoculated February 7. Series 1.*

Number.	Date.	Temperature.	Time.	Weight.	H ₂ O.	CO ₂ found.	Per Kilo per Hour.	O ₂ found.	Per Kilo per Hour.	R. Q.
1	April 9	23	9.55-10.55	26.8	grms.	grms.	grms.	grms.	grms.	
2	"	23	10.55-11.55	26.2	0.1095	0.1370	5.23	0.1055	4.03	0.95
3	"	23	11.55-12.55	25.8	0.2490	0.1160	4.46	0.1080	4.15	0.78
4	"	23	12.55-1.55	25.7	0.0660	0.1130	4.34	0.1165	4.51	0.71
					0.2030	0.1370	5.33	0.1425	5.56	0.70

April 8—Fed, 10.0-11.0 a.m. April 9—Fed on sop, 9.5-9.50 a.m. Tumour, size of walnut. Very ill.
 April 23—Killed with CHCl₃. Growth infiltrating peritoneum size of a walnut. Secondary deposits
 in both lungs. *Klossiella* in kidneys. No anyfold changes.